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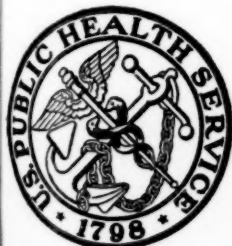
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FEDERAL SECURITY AGENCY
Oscar R. Ewing, Administrator

PUBLIC HEALTH SERVICE
Leonard A. Scheele, Surgeon General

Division of Public Health Methods
G. St. J. Perrott, Chief of Division

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Public Health Reports

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Siberian Tick Typhus

Relation of the Russian Strains to *Rickettsia prowazeki*

By T. T. CROCKER, B. L. BENNETT, E. B. JACKSON, M. J. SNYDER, J. E. SMADEL,
R. L. GAULD, and M. K. GORDON*

Siberian tick typhus (synonyms: tick-borne typhus, Far East typhus) has been recognized during the past 10 years as a disease entity caused by a rickettsia. Cases of this disease have been reported from Central Asia; Central Siberia (Krasnoyarsk area); and the Maritime Provinces (Khabarovsk area) of the Far East. It is an acute febrile illness which occurs in the spring and summer months, its incidence being closely related to the number and activity of ticks (1). East of Lake Baikal the vectors are believed to be *Haemaphysalis concinna* and *Dermacentor silvarum* (2, 3, 4, 5), while in Central Asia and Western Siberia the vector is said to be *Dermacentor nuttali* (1, 3, 5, 6, 7). It has been shown that the rickettsiae which are considered to be the etiological agents can be passed transovarially by these three species of ticks. The infection has also been transmitted to laboratory animals by the nymphs and larvae as well as by the adult ticks (2, 5, 6). Although these ticks parasitize a wide range of lower animal hosts, including rodents, birds, deer, horses, and cattle (4, 5), the actual reservoir of the rickettsia is not known. Savitskaia (11) has reported an isolation from the suslik, a type of ground squirrel.

Newer methods of antigenic analysis which have proved useful in establishing the relation of several of the recently isolated rickettsial agents, i. e., North Queensland tick typhus (8) and rickettsialpox (9) had not been applied to the agent of Siberian tick typhus. Therefore, it appeared worth while to subject several of the Russian strains to such tests. Accordingly, four strains purported to represent the rickettsiae of Siberian tick typhus were obtained from Russia through diplomatic channels during 1946-47. These agents were received at the Rocky Mountain Laboratory where they were used to establish infections in embryonated eggs and guinea pigs. Studies of these

*Department of Virus and Rickettsial Diseases, Army Medical Department Research and Graduate School, Army Medical Center, Washington, D. C.

strains were made both at the Rocky Mountain Laboratory and the Army Medical Department Research and Graduate School. This article describes the results obtained at the latter institution.

Clinical and Laboratory Findings Reported in Literature

A summary of Pletsity's (3) clinical description of Siberian tick typhus is as follows: Two or 3 days after being bitten by an infected tick, four out of five cases develop a lesion at the site of the bite. This consists of an area of infiltration $\frac{3}{4}$ to 1 inch in diameter surrounding an area of necrosis. At the same time there is regional lymphadenitis and possibly lymphangitis. After 3 or 4 days the infiltration subsides and the necrotic area becomes covered by a scab. Usually, the onset of constitutional signs and symptoms does not occur until after the acute localized manifestations have subsided; hence, the incubation period, between bite and generalized symptoms, is 8 to 11 days with a range from 6 to 16 days. The illness is characterized by headache, fever, pains in the extremities and, in some instances, vomiting. Typically a rash appears on the 3d day of fever, beginning on the upper extremities and extending over the entire skin surface. This eruption consists of large polymorphous rose-colored papules which remain discrete. These disappear in about 2 weeks without pigmentation or desquamation. The temperature ranges between 102° and 104° F. for 6 or 7 days before falling by lysis to normal levels between the 8th to 14th day after onset. As a rule, the patients do not appear acutely ill; neuropsychic symptoms are not marked; there are no cardiovascular signs or symptoms, and examination of the respiratory system reveals only a slight bronchitis. Convalescence is rapid, and most cases feel well a few days after the fever abates. The prognosis is good and there are no fatal cases on record. Abortive cases have been reported by Baidin (10). These fail to develop a rash and are often confused with grippe. A considerable number of cases give a history of a previous attack of epidemic typhus (3), usually occurring many years previously. There is no evidence that the disease is in any way modified in such patients.

A positive Weil-Felix test is obtained with the serum of some cases during the 1st week of illness, and almost all patients develop antibodies by the 10th or 12th day. Titers up to 1:6400 are found with OX19 antigen, and a titer of 1:400 may persist for as long as 3 months after recovery. Positive reactions are elicited with OX2 antigen but the titers are usually low, i. e., from 1:25 to 1:400. Frequently, however, a positive reaction appears earlier in the illness with the OX2 strain than with the OX19 organism. Sometimes positive tests with the OXK antigen appear late in the disease but then only at low titers.

Rickettsiae of Siberian tick typhus have been isolated from man, ticks, and rodents (1, 11) and have maintained their characteristics after passage for 50 generations in guinea pigs. Coincident with the febrile reaction, about 40 percent of infected male guinea pigs show swelling and edema of the scrotum which lasts 3 to 5 days. On the other hand, Korshunova (6, 12) working with strain G, Far East typhus, failed to obtain these scrotal reactions in inoculated male guinea pigs.

Four strains of the agent isolated in the Krasnoyarsk area of Central Siberia were found by Korshunova (1) to be immunologically identical. However, one of these, strain B, recovered from a human case, showed no cross-immunity with strain G from the Khabarovsk area. Furthermore, she reported strain G to be unrelated to the agents of epidemic typhus fever and boutonneuse fever. On the other hand, infection with strain B induced resistance to boutonneuse fever and infection with epidemic typhus resulted in some immunity to this strain. The reverse cross tests, however, gave negative results in both instances. A summary of Korshunova's findings is given in table 1.

Table 1. Cross-immunity tests in guinea pigs

Animals immune to	Challenge strain			
	Far East typhus (G)	Siberian tick typhus (B)	Epidemic typhus (Otto)	Boutonneuse fever
Far East typhus (G).....	+	0	0	0
Siberian tick typhus (B).....	0	+	0	+
Epidemic typhus (Otto).....	0	+	+	0
Boutonneuse fever.....	0	0	0	+

+ Immunity.

0 No immunity.

*Test indicates this immunity is partial only.

Material and Methods

Strains of Rickettsiae. All available data on the four strains of rickettsiae received from Russia are shown in table 2. Other rickettsiae used in the study were Breinl strain of epidemic typhus, Wilmington strain of murine typhus, Phillips strain of North Queensland tick typhus, Molish strain of South African tick bite fever, and the Bitter-root strain of Rocky Mountain spotted fever.

Infectious Inoculum. Two types of infectious inoculum were employed in the current study. Each of the four Russian strains received from the Rocky Mountain Laboratory was maintained by passage in yolk sacs of embryonated eggs and in guinea pigs. Infectious yolk sac tissue served as inoculum for embryos used in the preparation of vaccines and for complement-fixing antigens. Infectious guinea pig

materials, employed for passage of the strains and for challenge inocula, consisted of 10 percent suspensions of tissue or whole blood. The materials used in each case were epidemic typhus—brain; murine typhus—tunica washings; Siberian tick typhus—brain, or brain, spleen, and tunica mixture; North Queensland tick typhus and South African tick bite fever—spleen suspended in tunica washings; and Rocky Mountain spotted fever—heart blood.

Table 2. *History of four strains of agent of Siberian tick typhus fever rickettsia as received at Army Medical Department Research and Graduate School*

	Strain Designation			
	No. 1	No. 3	D11	XON
Original isolation.....	Krasnoyarsk area.	Khabarovsk area.	U. S. S. R.	U. S. S. R.
Original name.....	Strain B.....	Far East typhus Strain G.....	Strain D11.....	Strain XON.
Received in United States as.....	Lyophilized mouse lung.....	Lyophilized mouse lung.....	Not stated; prob- ably lyophilized mouse lung.....	Not stated; prob- ably lyophilized mouse lung.
Shipped to AMDRGS from Rocky Moun- tain Laboratory as...	Lyophilized guinea pig spleen and tunica.....	Lyophilized guinea pig spleen and tunica.....	Lyophilized yolk sac (4th egg pas- sage).....	Lyophilized yolk sac (4th egg pas- sage).
Date received at AMDRGS.....	Sept. 1946.....	Nov. 1946.....	July 1947.....	July 1947.

Technique of Cross-immunity Experiments. Groups of four to six guinea pigs which had been afebrile for at least 2 weeks after recovery from a typical clinical infection with one of the rickettsial agents served as immune animals for the test. These were then challenged by inoculation with 0.1 ml. of suspension of the appropriate rickettsial strain and at the same time groups of normal guinea pigs were also infected. After inoculation the animals were placed in an air-conditioned room and observed for 21 days during which period their temperatures were recorded daily. The response of the guinea pigs was measured by both the febrile and the scrotal reaction. A temperature recording of 104° F. or more was considered as fever and the febrile response of each group was recorded in two ways: (a) the number of animals showing fever and (b) the mean number of fever days in febrile animals. Scrotal reactions were also recorded both with respect to incidence and duration.

Vaccines. Two of four lots of vaccine used in the study were commercial preparations made from the Breinl strain of epidemic typhus. The other two were prepared in our laboratory from an egg-adapted line of the Siberian strain No. 3 in essentially the same manner used in the commercial manufacture of epidemic typhus vaccine, i. e., formalinized yolk sac suspensions which were extracted with ether to remove certain nonrickettsial materials.

Technique of Vaccination Tests. The appropriate vaccine was administered subcutaneously in two doses of 0.5 ml. each, given 7 days apart to groups of 10 male guinea pigs each weighing approximately 450 grams. Two weeks after the 2d dose the animals were challenged by inoculation with 0.1 ml. of a suspension containing one of the rickettsial strains and at the same time 10 nonvaccinated guinea pigs were given an equal amount of the same suspension. The reaction to infection was measured in the same manner as described for the cross-immunity experiments.

Complement Fixation Antigens and Antisera. Washed suspensions of *Rickettsia prowazeki* and *Rickettsia mooseri* prepared in the manner described by Plotz et al. (13) were used as complement-fixing antigen. Similar washed rickettsial antigens were prepared from the four Russian strains. Preparations containing soluble antigen free of intact rickettsia were prepared from materials designed for use as vaccines. These were subjected to high speed centrifugation and the resultant supernatant fluid served as soluble antigen. Antiserum was obtained by bleeding convalescent guinea pigs 2 to 4 weeks after recovery from induced infection with each of the rickettsial agents.

Technique of Complement Fixation Tests. Complement fixation tests were performed using the techniques regularly used in this laboratory (13). In brief, this method employed 0.25 ml. of diluted antigen, 0.25 ml. diluted serum, and 0.5 ml. of diluted fresh guinea pig serum containing two full units of complement. In determining the complement-fixing activity of unknown antigens, four units of antibody were added to serial dilutions of the material to be tested and, conversely, the sera to be tested were set up in serial dilution against two units of antigen. After incubation at 4° C. overnight, the hemolytic system was added and the test incubated at 37° C. for one-half hour and read in the usual manner. The data recorded in table 8 were obtained from tests which were all performed in one day, and the same antiserum and antigen from each strain were used throughout.

Results

Reaction of Guinea Pigs to Inoculation with Strains of the Agent of Siberian Tick Typhus. Guinea pigs inoculated with each of the four strains of Siberian tick typhus received at the Army Medical Department Research and Graduate School developed a similar febrile reaction which usually lasted from 4 to 6 days. No difference was noted in the ability of the different strains to cause scrotal reactions in adult male guinea pigs; and regardless of the strain employed, between 40 and 50 percent had swelling and edema of the scrotum. Stained smears from the tunica showed typical Mooser cells containing intracytoplasmic rickettsiae. In the course of these

studies, scrotal reactions appeared more frequently in guinea pigs infected with Siberian tick typhus than in those infected with the Breinl strain of epidemic typhus (28 percent). On the other hand, in these investigations the scrotal reaction did not appear as frequently with the Russian strains as with murine typhus (94 percent), South African tick bite fever (87 percent), North Queensland tick typhus (70 percent), and Rocky Mountain spotted fever (63 percent). Sera from guinea pigs convalescent from infection with any one of the four Russian strains contained complement-fixing antibodies which reacted with washed rickettsial antigens in a manner indistinguishable from that of serum of guinea pigs recovered from disease induced by the Breinl strain of epidemic typhus. Serological studies are discussed in some detail in a later paragraph.

The preliminary observations mentioned above seemed to indicate that the clinical aspects of the disease induced in this host by the Russian strains resembled experimental murine typhus more closely than experimental epidemic typhus; however, the antibody response of the animals convalescent from disease caused by the Russian strains was typical of epidemic typhus. At this stage of the investigations, the possibility was considered that these were "intermediate" strains of typhus such as have been reported to exist by other workers (14, 15). Since the technique of cross-vaccination is a well-recognized means of separating closely related but distinct rickettsial agents, it appeared advantageous to apply this method to the study of the relation of the Russian agents to epidemic typhus.

Cross-vaccination Experiments. Groups of guinea pigs were immunized with vaccines prepared against the Siberian strain No. 3 or with epidemic typhus vaccine and tested for resistance to infection

Table 3. *Protection against Siberian strain 3 induced by homologous vaccine and epidemic typhus vaccine*

Vaccinated with						Unvaccinated (controls)		
Siberian TT No. 3			Epidemic T vaccine					
Guinea pig number	Days fever	Days S. R.*	Guinea pig number	Days fever	Days S. R.*	Guinea pig number	Days fever	Days S. R.*
6599.....	0	0	6653.....	0	0	6717.....	3	1
6600.....	0	0	6654.....	0	0	6718.....	5	0
6601.....	0	0	6655.....	0	0	6719.....	6	0
6602.....	0	0	6656.....	0	0	6720.....	3	0
6603.....	0	0	6657.....	0	0	6721.....	8	1
6604.....	0	0	6658.....	0	0	6722.....	6	1
6605.....	0	0	6659.....	0	0	6723.....	5	1
6606.....	0	0	6660.....	0	0	6724.....	5	0
6607.....	0	0	6661.....	0	0	6725.....	4	0
6608.....	0	0	6662.....	0	0	6726.....	4	0
Total.....	0	0	Total.....	0	0	Total.....	49	4

* S. R. = Scrotal reaction.

NOTE: All animals were infected with a suspension of brain, spleen, and tunica tissues from guinea pigs suffering from disease induced by Siberian strain No. 3.

Table 4. Trivial protection against *R. mooseri* induced by Siberian and epidemic typhus vaccines

Vaccinated with						Unvaccinated (controls)		
Siberian TT No. 3			Epidemic T vaccine					
Guinea pig number	Days fever	Days S. R.*	Guinea pig number	Days fever	Days S. R.*	Guinea pig number	Days fever	Days S. R.*
6619.....	3	4	6683.....	2	1	6804.....	4	9
6620.....	3	3	6684.....	2	1	6805.....	4	8
6621.....	3	1	6685.....	1	2	6806.....	4	7
6622.....	2	4	6686.....	3	4	6807.....	4	6
6623.....	3	4	6687.....	3	4	6808.....	5	9
6624.....	4	5	6688.....	3	2	6809.....	5	9
6625.....	1	0	6689.....	2	0	6810.....	6	5
6626.....	3	4	6690.....	1	0	6811.....	4	6
6627.....	1	0	6691.....	1	0	6812.....	3	5
6628.....	3	2	6692.....	2	5			
Total.....	26	27	Total.....	20	19	Total.....	39	64

*S. R. = Scrotal reaction.

with one of the Russian strains or with other rickettsial agents. Results typical of those obtained in these studies are summarized in tables 3 and 4. The former presents the data from an experiment in which the animals were challenged by infection with Siberian strain No. 3. Both groups of vaccinated guinea pigs were completely protected against this Russian strain. In this test, each of the control animals displayed a febrile response and some developed a mild scrotal reaction. The failure of the Siberian and epidemic typhus to induce appreciable protection against the agent of murine typhus is indicated by the data presented in table 4. Here guinea pigs immunized with the same materials employed in the experiment summarized in table 3 were infected with *R. mooseri* and all animals, both vaccinated and control, developed fever. The duration of the febrile reaction and the incidence and duration of the scrotal reaction was, however, less among the vaccinated than among the control animals.

An interpretative summary of all of the findings in the cross-vaccination experiments is shown in table 5. Regardless of whether the vaccine used was prepared from organisms of epidemic typhus or the Siberian strain No. 3, the vaccinated guinea pigs showed essentially the same amount of protection when infected with a given rickettsial agent. Furthermore, vaccines prepared from either strain induced equal resistance against infection with the Breinl strain of epidemic typhus fever and all four strains of Siberian tick typhus. Moreover, the degree of resistance induced by vaccination with the Siberian strain against subsequent infection with *R. mooseri* was of the same order as that induced by epidemic typhus vaccine. Vaccination against Siberian strain No. 3 afforded no protection against either North Queensland tick typhus or South African tick bite fever.

Table 5. Interpretative summary of results of cross-vaccination tests

Challenge	Vaccine			
	Epidemic typhus		Siberian TT No. 3	
	Lot No. 1	Lot No. 2	Lot No. 1	Lot No. 2
Epidemic typhus.....	++	++	++	++
Siberian No. 1.....	+	+	+	+
Siberian No. 3.....	+	+	+	+
Siberian XON.....		+		+
Siberian D11.....		+		+
North Queensland tick typhus.....				0
South African tick bite fever.....				0
Murine.....		+		+

++ Complete or almost complete protection.

+ Partial protection.

0 No protection.

Cross-immunity Tests. Guinea pigs, recovered from infection with one of the Siberian strains or one of the rickettsial agents commonly employed in this laboratory, were tested for resistance to infection with a number of heterologous organisms. The results of a typical cross-immunity experiment are presented in table 6. In this particular test, guinea pigs convalescent from one of the four strains of Siberian tick typhus were injected with the Breinl strain of epidemic typhus. It will be seen that all of the recovered animals were im-

Table 6. Resistance of Siberian immune guinea pigs to epidemic typhus

Guinea pig number	Initial infection		Epidemic typhus challenge	
	Siberian strain	Days fever	Days fever	Days scrotal reaction
6800.....	No. 1.....	4	0	0
6801.....	No. 1.....	0	4	0
6802.....	No. 1.....	5	0	0
6745.....	No. 1.....	2	0	0
6849.....	No. 3.....	2	0	0
6850.....	No. 3.....	5	0	0
6768.....	No. 3.....	8	0	0
6720.....	No. 3.....	3	0	0
6755.....	No. 3.....	2	1	0
6778.....	No. 3.....	3	0	0
6765.....	XON.....	2	0	0
6766.....	XON.....	1	0	0
6779.....	XON.....	1	0	0
6707.....	XON.....	4	0	0
6708.....	XON.....	5	0	0
6709.....	XON.....	6	0	0
6817.....	D11.....	7	0	0
6818.....	D11.....	6	0	0
6823.....	D11.....	6	0	0
6837.....	D11.....	7	0	0
6783.....	D11.....	4	0	0
6975.....	None.....		6	2
6976.....	None.....		7	0
6977.....	None.....		2	0
6998.....	None.....		6	1
6979.....	None.....		6	1
6980.....	None.....		7	0

immune to *R. prowazeki*. In one instance, guinea pig No. 6801, which had failed to develop fever following inoculation with Siberian strain No. 1, did show a febrile response lasting 4 days when injected with the organism of epidemic typhus. This animal, however, cannot be considered as having been immune to Siberian tick typhus.

The results of the entire series of cross-immunity tests are summarized in schematic form in table 7. A review of this table shows that complete cross-immunity exists between all the Siberian strains and the Breinl strain of epidemic typhus. All five of these strains also behaved similarly in that they induced considerable immunity against the Wilmington strain of murine typhus. Guinea pigs convalescent from murine typhus were solidly protected against infection with the four Siberian strains. No cross-immunity was demonstrable between the strains of Siberian tick typhus and the agent of Rocky Mountain spotted fever.

The results of cross-immunity tests presented no evidence of a relationship between North Queensland tick typhus and South African tick bite fever and the Siberian strain No. 3. However, D11 and XON infections elicited questionable or partial resistance against both North Queensland tick typhus and South African tick bite fever and guinea pigs convalescent from these two latter infections were partially protected against infection with D11 and XON.

Complement Fixation Tests. The extremely close relation of the Siberian strains to *R. prowazeki* indicated in the earlier complement fixation tests as well as by cross-vaccination and cross-immunity tests led us to investigate the interrelation between these agents by means of complement fixation technique in greater detail. Accordingly, suspensions of washed rickettsiae of the four Russian strains

Table 7. Summary of results of cross-immunity tests

Type of immune guinea pigs	Challenge agent							
	Epidemic typhus (Breinl)	Siberian TT No. 1	Siberian TT No. 3	Siberian TT D11	Siberian TT XON	Murine typhus (Wilmington)	Rocky Mt. spotted fever	NQTT SATBF
Epidemic typhus (Breinl)	---	++	++	++	++	+	+	---
Siberian tick typhus No. 1	++	---	++	++	++	+	0	0
Siberian tick typhus No. 3	++	++	---	++	++	+	0	0
Siberian tick typhus D11	++	++	++	---	++	++	0	+
Siberian tick typhus XON	++	++	++	++	---	+	0	+-
Murine typhus (Wilmington)	---	---	---	---	---	---	---	---
Rocky Mountain spotted fever	---	++	++	++	++	---	---	---
North Queensland tick typhus	---	0	0	+	+	---	---	---
South African tick bite fever	---	+	0	+	+	---	---	---

++ Solid immunity.

+ Partial immunity.

+- Questionable immunity.

0 No immunity.

Table 8. *Cross-reactions between Siberian, epidemic and murine typhus as demonstrated by complement fixation*

Antibody (4 units)	Antigens					
	Siberian TT No. 1	Siberian TT No. 3	Siberian TT D11	Siberian TT XON	Epidemic typhus (Breinl)	Murine typhus (Wilmington)
	Antigen titers					
Siberian tick typhus No. 1.....	80	80	120	30	240	40
Siberian tick typhus No. 3.....	80	80	120	40	240	negative*
Siberian tick typhus D11.....	80	60	120	40	320	Do
Siberian tick typhus XON.....	80	80	120	40	320	Do
Epidemic typhus.....	80	80	120	30	320	Do
Murine typhus.....	30	15	30	10	negative*	320

*Lowest dilution tested 1:40.

were prepared and these together with our standard epidemic and murine typhus antigens were titrated with their respective homologous convalescent guinea pig sera. On the basis of these titrations the dilution of antiserum was selected which contained four units of antibody against the homologous antigen. These chosen dilutions of antisera were then used in constant amounts with serial dilutions of each antigen in order to determine the titer of each antigen in the presence of homologous and heterologous antibodies. The results of these tests are summarized in table 8. The findings indicate that the four Siberian strains and the Breinl strain of epidemic typhus are indistinguishable from each other. Furthermore, the Russian and Breinl strains behaved similarly in their cross-reactions with the Wilmington strain of murine typhus.

Crude preparations of soluble antigen were made from yolk sac material infected with the four Russian strains and with the standard epidemic and murine organisms. These were employed in cross complement fixation tests in the manner described in the preceding paragraph for washed rickettsial antigens. The same antisera were used in both instances. As was to be expected, the soluble antigens from the Russian strains were indistinguishable from one another and from the epidemic and murine typhus materials.

Discussion

The results of cross-vaccination, cross-immunity, and complement fixation tests indicate that the four Siberian strains are identical and cannot be differentiated from each other by any of these means. They are identical, moreover, with the Breinl strain of epidemic typhus fever. In addition, the Russian agents show a relation to the Wilmington strain of murine typhus which is similar to that displayed by a classical strain of epidemic typhus.

Cross-vaccination and cross-immunity experiments indicate that

guinea pigs either vaccinated against Siberian strain No. 3 or convalescent from infection with this strain are not protected against infection with the organisms of either North Queensland tick typhus or South African tick bite fever. However, clinical infection with the D11 and XON Siberian strains gave partial protection against these rickettsiae, and infection with North Queensland tick typhus both and South African tick bite fever made guinea pigs partially immune to infection with the D11 and XON strains. It should also be noted that infection with South African tick bite fever made guinea pigs partially immune to infection with Siberian strain No. 1, but Siberian strain No. 1 immune guinea pigs were susceptible to South African tick bite fever. Similar findings have been encountered in cross-immunity tests with various rickettsiae. For example, guinea pigs convalescent from Rocky Mountain spotted fever are partially resistant to infection with murine and epidemic typhus and, conversely, typhus-immune guinea pigs are resistant to Rocky Mountain spotted fever (16, 17). There is similar resistance to cross-infection with North Queensland tick typhus, South African tick bite fever, and murine typhus (8).

Summary and Conclusions

1. Four strains of rickettsiae, supposedly the etiological agents of Siberian tick typhus, have been studied and their relation to one another and to other rickettsiae determined by means of cross-vaccination, cross-immunity, and complement fixation tests.

2. All four strains were found to be indistinguishable from each other and the Breinl strain of epidemic typhus.

3. It is apparent that the cross-immunity reactions displayed by the four Siberian strains in the current tests are distinctly different from those attributed to them by the Russian investigators who themselves report divergent results. Various hypotheses might be offered to explain these differences, but such theorizing appears fruitless. Whether the Siberian strains received here bear an etiological relation to the clinical disease designated as Siberian tick typhus is uncertain. However, if they represent the causal agent of Siberian tick typhus, it is interesting to speculate on the possibility of *R. prowazeki* being maintained by a rodent-tick cycle in nature. This would leave man as only an incidental host who might, under the proper circumstances, start an epidemic of classical louse-borne typhus.

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Q Fever Studies in Southern California

XI. Recovery of *Coxiella burnetii* from Milk of Sheep

By W. L. JELLISON, PH. D., H. H. WELSH, M. S., B. E. ELSON, D. V. M.,
and R. J. HUEBNER, M. D.*

Epidemiological studies of Q fever in southern California (1) indicated that dairies and dairy cows were sources of human infection in that area, while epizootological studies showed that large numbers of dairy cows were infected with the disease and were shedding rickettsiae in their milk (2). Although dairying is the most extensive livestock industry in Los Angeles County, there are also goat farms, sheep, extensive cattle feeding yards, hog feeding yards, race horse stables, and riding academies. Raising of small animals, such as rabbits, chickens, and turkeys, is also a widespread activity. There are numerous meat packing plants for processing cattle, sheep, and hogs. Some of the cases of Q fever were employees at the Union Stock Yards, at meat packing plants, and at rendering plants, where exposure to a variety of animals, including dairy cows, was a regular experience. Although studies of goats and sheep were not exhaustive and were secondary to the extensive studies of cattle, nevertheless, these possible sources of infection in southern California were considered.

Histories of 300 human cases of Q fever (1) suggested sheep or goats as a possible or probable source of infection in only 6 instances. This is in contrast to the observations of Lennette, Clark, and Dean (3) in northern California where 81 of 150 confirmed cases had close and frequent contact with sheep and goats; and of Caminopetros (4) in Greece where goats and sheep are abundant. Recovery of *Coxiella burnetii* from milk of sheep has been reported by both groups.

Human Cases

The following cases, confirmed by complement fixation tests on serum samples using a specific Q fever antigen, gave a history of contact with sheep, this contact being considered as a possible source of infection:

H. S., a male aged 30, of Placentia, had lived in southern California 3½ years. He was employed as a correctional officer at the Chino

*Rocky Mountain Laboratory, Hamilton, Mont.; Viral and Rickettsial Disease Laboratory, California State Department of Public Health, Berkeley, Calif.; California State Department of Agriculture, Berkeley, Calif.; and the Laboratory of Infectious Diseases, National Institutes of Health, respectively.

This work was facilitated by the Q Fever Laboratory, which was established September 12, 1947, in the endemic area of southern California, as a cooperative undertaking of the National Institutes of Health, the California State Departments of Public Health and Agriculture, and the Los Angeles County and City Health Departments.

State Institution for Men, Chino, California. Cows and other livestock were kept on the farm at this institution. About 14 days before onset of illness he had watched the unloading from trucks of a flock of sheep at the institution. These were mostly old ewes recently separated from their lambs and had been trucked in from Kern County, California. This patient also used raw milk regularly from a neighbor's cow. He was taken ill June 26, 1948, and admitted to the Fullerton General Hospital 3 days later with the diagnosis of "fever of unknown origin." A blood sample taken June 27 was negative for Q fever antibodies, but specimens taken July 6 and July 12 were both positive for Q fever at high titer (4+ at 1:64, the highest dilution tested) when tested at the National Institutes of Health.

E. C., a male aged 41, was living at El Monte, California, but worked shearing sheep at Ocean Side, California, 10 days before becoming ill. He was admitted to the Los Angeles General Hospital May 6, 1948, with a tentative diagnosis of Q fever. A blood sample taken May 14 was negative for Q fever and a sample taken 1 week later, May 21, was positive (3+ at 1:64). Both samples were tested at the Viral and Rickettsial Disease Laboratory, Berkeley, California.

On July 18, 1948, 128 sheep in the flock to which H. S. was exposed were bled, and the serums were tested at the National Institutes of Health by the complement fixation test for Q fever. Only 33 of the 128 sheep were completely negative. However, only 13 gave reactions usually regarded as significantly positive, that is 3+ at 1:8 or higher. Eighty-two sheep gave partial reactions less than 3+ at 1:8.

None of the samples was positive at a dilution of greater than 1:16. Such a large proportion of weak reactions has not been experienced in similar surveys of bovine herds, although more than 20,000 bovine samples have been tested. We do not have results on a sufficient number of sheep sera from this or other areas to properly interpret these results. It seems likely that the hemolytic test system used, consisting of sheep red cells and antish sheep cell amboceptor, may give some nonspecific reactions when sheep serums are tested. However, the 13 reactions in serum dilutions of 1:8 and 1:16 in the test, as run at the National Institutes of Health, is suggestive of specific antibodies for Q fever.

Tests of Lacteal Secretions

This herd of ewes had been separated from their lambs more than 2 months. Lacteal secretion samples from 104 of the 128 ewes were combined in a total of 13 pooled samples representing from 5 to 10 sheep each.

For preliminary testing, two composite samples (A and B) were

prepared, each of which contained milk from 52 sheep. The remaining pooled samples were frozen and stored below freezing temperature.

Each composite sample was tested by injecting two normal guinea pigs with 4 cc. intraperitoneally and 1 cc. subcutaneously. These animals were bled after a 30-day period, and their serums were tested by the complement fixation technique. One animal that received milk from composite A was positive at 1:64, the highest dilution tested. The other animal that received milk from composite A and both animals that received milk from composite B gave weak reactions of questionable significance. Portions of both composite samples of sheep milk were sent under refrigeration to the Rickettsial Laboratory at the National Institutes of Health where they were tested in guinea pigs with negative results.

After receipt of these results, the 13 pool samples were then removed from cold storage and each was tested in two guinea pigs in a similar manner. A normal control animal was kept in the cage with each pair of injected guinea pigs.

Three of the 26 injected animals died of undetermined causes before the 30-day test period was completed. The remaining 23 and the 13 controls were bled at the end of the 30 days and their serums were tested for Q fever antibodies by complement fixation. Nineteen animals representing 11 pools of sheep milk and all of the 13 control animals were entirely negative. One guinea pig that received milk from pool 4 was positive by complement fixation test at a titer of 1:64, the highest dilution tested. Its mate gave a moderately high titer, showing complete fixation at 1:32; 2+ at 1:64. One animal that received milk from pool 12 was positive at a titer of 1:64 and its mate was negative. These reactions are summarized as follows:

Sheep milk pool	Guinea pig	Complement* fixation titer 30 days after injection
4-----	{ 96, 149	4+ at 1:64.
	{ 96, 150	2+ at 1:64.
	{ 96, 173	4+ at 1:64.
12-----	{ 96, 174	Negative in all dilutions.

Milk of pool 4 was reinjected in three guinea pigs. One animal died; one was positive by complement fixation test after a 30-day interval; and the third animal was sacrificed and tissues were passed to two fresh animals. One of these was held for 30 days and was positive by complement fixation test. The other was sacrificed on the 10th day and tissues sent to the National Institutes of Health where the strain was successfully maintained through six additional animal passages, established in chick embryo cultures, and identified as *Coxiella burnetii* (Derrick). This strain has been designated as the "chino" strain.

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Further confirmation that this strain of infection was Q fever was made by reciprocal cross-immunity tests with the Dyer strain of Q fever, which was isolated in 1938 (5) from a human case of the disease. The results of these cross-immunity tests are summarized in the table.

Cross-immunity tests of "sheep" strain with Dyer strain in guinea pigs

Animal No.	Recovered from—	Challenge strain	Date inoculated	Days incubation	Days fever
A					
41882	Dyer strain	Sheep-milk strain	1949 Feb. 11	21	0
41883	do.	do.	do.	21	0
41599	do.	do.	Feb. 17	21	0
41600	do.	do.	do.	21	0
B					
43653	Normal control	Sheep-milk strain	Feb. 11	3	4
43654	do.	do.	do.	4	2
43655	do.	do.	do.	4	3
43656	do.	do.	do.	4	3
43657	do.	do.	Feb. 17	6	1
43658	do.	do.	do.	6	1
C					
43582	Sheep-milk strain	Dyer Q	Mar. 28	21	0
43653	do.	do.	Mar. 21	21	0
43655	do.	do.	Mar. 28	21	0
43656	do.	do.	Mar. 21	21	0
D					
44233	Normal control	Dyer Q	Mar. 21	3	6
44234	do.	do.	do.	3	5
44235	do.	do.	do.	6	4
44236	do.	do.	do.	3	4
44249	do.	do.	Mar. 28	3	7
44250	do.	do.	do.	3	7
44251	do.	do.	do.	3	7
44252	do.	do.	do.	3	4

Four guinea pigs, which had recovered from infection with the Dyer strain, and six normal controls were injected intraperitoneally with 2 cc. of a spleen and liver suspension from guinea pigs infected with the sheep-milk strain. Animals recovered from the Dyer strain remained afebrile for a period of 21 days. Each of the six normal animals given the sheep-milk strain of inoculum developed 1 to 4 days of fever after incubation periods of 3 to 6 days.

Four of the animals which had recovered from the sheep-milk strain of infection were challenged with the Dyer strain of Q fever by receiving intraperitoneally 2 cc. of spleen and liver tissue suspension from infected guinea pigs. All four animals remained afebrile, whereas each of the eight normal controls receiving similar injections developed 4 to 7 days of fever after incubation periods of 3 to 6 days.

The clots from the blood samples of these sheep had been saved in a frozen condition and were likewise tested by guinea pig injection upon obtaining positive tests from the composite milk samples. Clots from each 10 sheep were pooled, macerated, and injected into two animals. A normal control was maintained with each pair of test animals. Thirteen test animals and two controls died before the 30-day test period was completed. The 13 surviving test animals and

11 controls bled on the 30th day were all negative for Q fever by the complement fixation test.

Summary

Two of 300 cases of Q fever in southern California gave histories of contacts that specifically suggested sheep as a source of infection.

Low titrated reactions with Q fever antigens were demonstrated in the complement fixation test by serums of sheep from one flock. Lacteal secretions from these sheep produced Q fever in test animals, and a strain of *Coxiella burnetii* was established in guinea pigs and was identified by accepted criteria.

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Cultivation of Fixed Rabies Virus in Embryonated Duck Eggs

By H. M. POWELL, Sc. D., and C. G. CULBERTSON, M. D.*

In the last few months we have experimented with cultivation of fixed rabies virus in embryonated duck eggs apparently with at least a moderate degree of success.

In this work we have used mainly a strain of rabies virus known in this laboratory as "N. I. H.," and originally obtained from the National Institutes of Health. We have also used strains "H. L.," "Park," "Phillips," and "Harris." These strains were obtained from the Rabies Vaccine Department of this laboratory. A stock of mouse brain virus of the different viruses served as seed virus.

The fertile duck eggs used were first incubated 7 days at about 37° C. At this time, they were injected with doses of 0.2 cc. of 10⁻² dilutions of rabies seed virus in the same way that embryonated hen eggs are infected with influenza virus. The 7-day inoculated duck eggs were incubated an additional 14 days at about 35° to 36° C. At this time, the sterile embryos were recovered in the usual way, weighed, and spun 2 or 3 minutes in a Waring Blendor with sufficient physiological salt solution to make a 1:10 dilution.

Intracerebral mouse tests were conducted with decimal dilutions of duck embryo virus. At this writing, 3 serial passages of N. I. H. duck embryo virus have been made in duplicate lines of passage. The results of these tests are as follows:

Virus dilution	Passages					
	1A	1B	2A	2B	3A	3B
10 ⁻¹	6, 6	5, 7	6, 6	6, 6	7, 7	5, 6
10 ⁻²	6, 7	6, 7	6, 6	6, 7	7, 8	7, 8
10 ⁻³	6, 9	6, 6	6, 6	7, 8	8, 10	9, ?
10 ⁻⁴	6, 8	8, 9	6, 6	9, S	8, 10	9, 9
10 ⁻⁵	--	9, 9	6, 8	8, 10	7, S	S, S
10 ⁻⁶	--	5, 9	7, 8	10, S	S, S	S, S
10 ⁻⁷	--	--	7, S	S, S	S, S	S, S
10 ⁻⁸	--	--	8, S	S, S	S, S	S, S

NOTE.—Each figure indicates day of death of 1 mouse; S indicates survival 14 days; -- indicates not done

Aside from the N. I. H. strain, the other four strains of rabies virus mentioned have been subjected to attempted passage in duck embryo-onated eggs 1, 2, or 3 times for the different strains, and duck embryo

*Lilly Research Laboratories, Indianapolis.

virus titers of 10^{-3} to 10^{-5} have been obtained. In addition to virus titers in the embryo proper, titers of 10^{-2} or slightly more have been noted in some of the periembryonic fluids.

Of the duck embryo rabies virus strains, the N. I. H. strain in duck passage 2 has been found to be neutralized specifically by rabbit anti-rabies serum (anti-H. L. strain) furnished by Dr. MacFarlane of this laboratory. The other strains have not been tested. The N. I. H. duck embryo virus (the only one tested) has produced in two rabbits, following intracerebral injection, the usual symptoms and death occurring after customary rabbit injection of rabbit fixed rabies virus.

The N. I. H. strain of duck embryo pooled passage two rabies virus was used for vaccinating mice as a vaccine potency test according to National Institutes of Health test methods. A 1:20 dilution of active stock 1:10 virus (0.5 percent suspension) was used for intraperitoneal mouse doses of 0.25 cc. each. Six doses were given during two weeks, i. e., on Monday, Wednesday, and Friday of each week, and on Monday after the last Friday's dose, the mice were challenged intracerebrally with decimal dilutions of the N. I. H. strain of mouse brain virus. The results were as follows:

<i>Virus dilution</i>	<i>Immunized mice</i>	<i>Control mice</i>
10^{-1}	(1), (1), 6, 9, 9, 11, 11, S, S, S	6, 7, 7, 7, 7, 7, 8, 8, 8
10^{-2}	(1), 6, 10, 12, 13, S, S, S, S, S	7, 8, 8, 8, 8, 8, 8, 8, 9, 9
10^{-3}	7, 9, 11, 11, 12, 12, 12, S, S, S	7, 7, 8, 8, 8, 8, 8, 9, 9, 10
10^{-4}	8, S, S, S, S, S, S, S, S, S	8, 8, 9, 9, 9, 9, 9, 9, 10
10^{-5}	13, S, S, S, S, S, S, S, S, S	8, 8, 9, 9, 10, 10, 10, 11, S, S
10^{-6}	—	7, 7, 8, 8, 10, S, S, S, S, S
10^{-7}	—	7, 8, 8, S, S, S, S, S, S, S

NOTE.—Each figure indicates day of death of 1 mouse; S indicates survival 14 days; — indicates not done

It is computed that the immunized mice resisted 7,700 LD₅₀ of challenge virus.

At this writing, additional immunization tests are being done in mice. Also, further transmission of the virus in embryonated duck eggs is being tried, and other problems which obviously suggest themselves are being studied.

This preliminary note is published so that others who may be particularly interested in this virus can try such experiments without delay.

INCIDENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED MARCH 4, 1950

The reported incidence of influenza in the Nation increased for this week from 14,556 cases last week to 24,705. The 5-year (1945-49) median is 5,337. The cumulative total for the first 9 weeks of the year is 88,901 as compared with the corresponding cumulative total of 41,359 for 1949, and a 5-year (1945-49) median of 41,359.

Increases over the previous week in reported cases of influenza were shown in all the geographic divisions except the New England and Pacific Divisions, with the largest being in the South Atlantic Division (from 3,469 to 7,047). For most of the individual States, increases were reported. Some of the larger increases were in Alabama (from 295 to 638), Arkansas (from 297 to 516), Colorado (from 226 to 612), Georgia (from 209 to 443), Kentucky (from 27 to 358), Montana (from 383 to 1,541), Oklahoma (from 543 to 1,297), Tennessee (from 123 to 654), Texas (from 8,549 to 10,738), and Virginia (from 2,377 to 5,524). A few States showed no change and six States reported decreases.

Increases over last week may be noted in reported cases of pneumonia (2,457 to 3,118), measles (8,172 to 9,584), meningococcal meningitis (85 to 87), scarlet fever (1,862 to 1,938), and whooping cough (2,447 to 2,962). New Jersey reported 1,022 cases of measles as compared with 494 last week, and a 5-year (1945-49) median of 993. Other States reporting increases in reported cases of measles were Massachusetts (165 to 306), Minnesota (57 to 219) and New York (561 to 958).

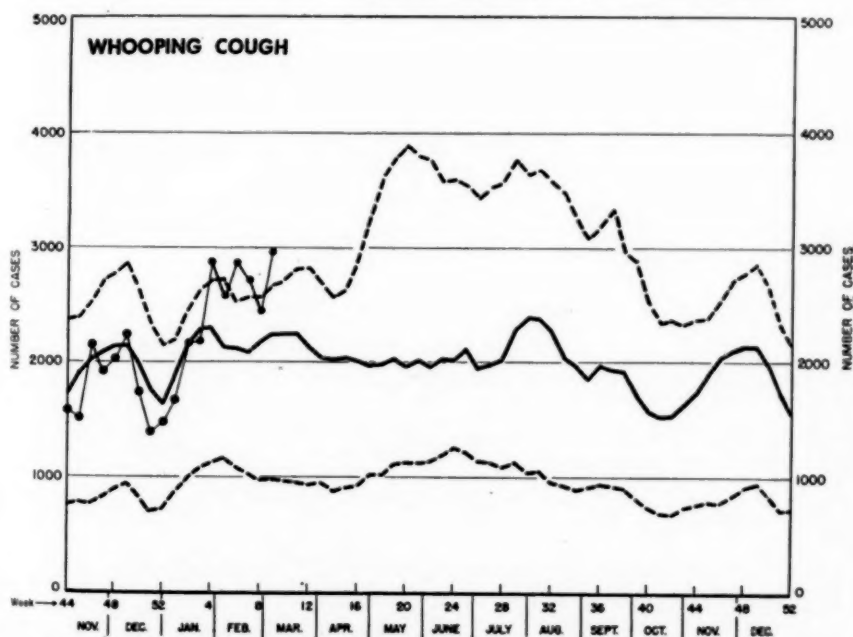
Decreases from the previous week occurred in diphtheria (149 to 143), poliomyelitis (97 to 82), typhoid and paratyphoid fever (46 to 45), and rabies in animals (168 to 151).

Two cases of smallpox were reported in the United States, one each in Arkansas and Oklahoma.

A total of 10,218 deaths was recorded during the week in 93 large cities in the United States as compared with 9,470 last week and a 3-year 1947-49 median of 9,712. For the year to date the total is 86,413 as compared with 88,112 for the corresponding period last year.

Communicable Disease Charts

All reporting States, November 1949 through March 4, 1950



The upper and lower broken lines represent the highest and lowest figures recorded for the corresponding weeks in the 5 preceding years. The solid line is a median figure for the 5 preceding years. All three lines have been smoothed by a 3-week moving average. The dots represent numbers of cases reported for the weeks, 1949-50.

March 24, 1950

Telegraphic case reports from State health officers for the week ended March 4, 1950

[Leaders indicate that no cases were reported]

Division and State	Diphtheria	Encephalitis, infectious	Influenza	Measles	Meningitis, meningococcal	Pneumonia	Polio-myelitis	Rocky Mountain spotted fever	Scarlet fever	Small-pox	Tularemia	Typhoid and paratyphoid fever	Whooping cough	Rabies in animals
NEW ENGLAND														
Maine.....	2	11	5	7	34
New Hampshire.....	6	2	4
Vermont.....	6	1	5	10
Massachusetts.....	6	366	1	105	3	117
Rhode Island.....	1	1	11	2	38
Connecticut.....	17	40	1	24	2	122
MIDDLE ATLANTIC														
New York.....	6	3	18	958	7	283	9	150	1	189	10
New Jersey.....	2	1	7	1,022	2	120	1	69	173
Pennsylvania.....	7	369	4	188	127	1	199	1
EAST NORTH CENTRAL														
Ohio.....	11	7	258	7	96	2	329	1	199	8
Indiana.....	6	2	25	173	22	1	74	1	36	8
Illinois.....	3	160	7	98	2	79	2	89	1
Michigan.....	5	8	2,492	1	44	4	175	1	1	300	4
Wisconsin.....	80	334	1	20	88	120
WEST NORTH CENTRAL														
Minnesota.....	9	219	1	4	2	25	40	1
Iowa.....	35	636	3	35	1	16	11
Missouri.....	12	8	2	27	46
North Dakota.....	1	2	73	4	1	106	7	1	1	3
South Dakota.....	3	20	6
Nebraska.....	16	162	1	6	1	9	10
KANSAS.....	1	190	9	17	1	25	32
SOUTH ATLANTIC														
Delaware.....	33
Maryland.....	6	15	33	1	45	7	10
District of Columbia.....	90	29	56	1	82
Virginia.....	6	55	2	156	17	4	2
West Virginia.....	11	5,524	131	1	25	1	21	1	40	2
North Carolina.....	5	974	187	1	35	86	11
South Carolina.....	1	51	2	12	2	7	2	76	7
Georgia.....	7	88	40	1	185	1	1	7	4	20
Florida.....	2	443	27	2	8	2	1	1	2	29	6
EAST SOUTH CENTRAL														
Kentucky.....	10	3

PLAGUE INFECTION IN EDDY COUNTY, NEW MEXICO

Under date of March 3, plague infection was reported proved in 8 fleas, *Thrassius fatus*, taken from 5 grasshopper mice, *Onychomys leucogaster*, trapped February 16, 1950, along U. S. Highway 83, 2 miles west of Loco Hills, Eddy County, New Mexico.

FOREIGN REPORTS

CANADA

Provinces—Notifiable diseases—Week ended February 11, 1950— During the week ended February 11, 1950, cases of certain notifiable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	New-found-land	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox.....	2		14		266	331	38	38	79	130	898
Diphtheria.....				1	3	2					6
Dysentery:											
Amebic.....						1					1
Bacillary.....					5	1					8
German measles.....			53		11	278	1	44	334	408	1,129
Influenza.....			19			19	7			4	49
Measles.....			11		158	723	37	54	81	133	1,197
Meningitis, meningococcal.....							1				1
Mumps.....			82		470	667	14	59	79	449	1,820
Scarlet fever.....	3		4	1	65	49	18		70	16	226
Tuberculosis (all forms).....	24			19	98	32	8	8	124	51	364
Typhoid and paratyphoid fever.....					12	2			2		16
Undulant fever.....					5	1					6
Venereal diseases:											
Gonorrhea.....	7	2	24	9	89	48	20	10	52	70	331
Syphilis.....	5		4	3	106	36	5	9	1	19	188
Whooping cough.....			9		79	77	11	13	2	18	209

FINLAND

Notifiable diseases—January 1950— During the month of January 1950, cases of certain notifiable diseases were reported in Finland as follows:

Disease	Cases	Disease	Cases
Diphtheria.....	69	Typhoid fever.....	8
Meningitis, meningococcal.....	13	Venereal diseases:	
Paratyphoid fever.....	83	Gonorrhea.....	537
Poliomyelitis.....	12	Syphilis.....	54
Scarlet fever.....	820		

JAPAN

Influenza—During the week ended February 11, 1950, 2,746 cases of influenza were reported in Japan.

MEXICO

Poliomyelitis—During the period January 15 to February 11, 1950, 20 cases of poliomyelitis were reported in Mexico City, and for the period January 22 to February 11, 7 cases were reported in Monterrey.

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

Note.—The following reports include only items of unusual incidence or of special interest and the occurrence of these diseases, except yellow fever, in localities which had not recently reported cases. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

Cholera

India—During the week ended February 25, 1950, cholera was reported in India as follows: Cuddalore, six cases; Madras, one case; Masulipatam, three cases; Negapatam, two cases; Tuticorin, two cases.

Plague

Ecuador—Loja Province—During the week ended January 3, 1950, one case of plague was reported in Celica County, Loja Province.

Siam (Thailand)—During the week ended February 11, 1950, three cases of plague were reported in Siam.

Smallpox

Burma—During the week ended February 25, 1950, 100 cases of smallpox were reported in Bassein and 122 cases were reported in Rangoon.

India—During the week ended February 25, 1950, 33 cases of smallpox were reported in Bombay, 22 cases in Delhi, and 305 cases in Madras.

Mexico—During the period January 15 to February 11, 1950, 14 cases of smallpox were reported in Mexico City.

Typhus fever

Japan—During the week ended February 25, 1950, 61 cases of typhus fever were reported in Yokohama, and 35 cases in Tokyo.

Yellow fever

Bolivia—Under date of February 18, 1950, 70 cases of yellow fever with 15 deaths were reported in Chiquisaca Department, Bolivia.

Gold Coast—During the week ended January 11, 1950, one case of yellow fever was reported at Ankobra Junction Station; hospitalized in Bogoso.

DEATHS DURING WEEK ENDED MAR. 4, 1950

	Week ended Mar. 4, 1950	Correspond- ing week, 1949
Data for 93 large cities of the United States:		
Total deaths.....	10,218	9,712
Median for 3 prior years.....	9,712
Total deaths, first 9 weeks of year.....	86,413	88,112
Deaths under 1 year of age.....	667	627
Median for 3 prior years.....	671
Deaths under 1 year of age, first 9 weeks of year.....	5,618	5,985
Data from industrial insurance companies:		
Policies in force.....	69,844,153	70,565,749
Number of death claims.....	14,508	13,645
Death claims per 1,000 policies in force, annual rate.....	10.8	10.1
Death claims per 1,000 policies, first 9 weeks of year, annual rate.....	9.8	9.6

World Health Day

The United States is joining with more than 60 nations in the international observance of World Health Day on April 7. In connection with the United States observance, the Division of International Health, Public Health Service, has prepared information kits providing background material on international health activities. This material will be useful to those desiring to take part in local observances. The kits will be distributed to State and local health officers on the basis of requests received. Please address requests, indicating the number of kits desired, to Dr. L. L. Williams Jr., Chief, Division of International Health, Public Health Service, Federal Security Agency, Washington, D. C.

The information kits will include the following items: (1) statement by Dr. Brock Chisholm, Director General of the World Health Organization; (2) statement by Federal Security Administrator Oscar R. Ewing; (3) statement by Surgeon General Leonard A. Scheele; (4) pamphlet on the World Health Organization; (5) article on United States participation in world health programs; (6) Working for World Health (excerpts from annual report of Public Health Service); (7) Improved Health Conditions in Europe from an address by Senator Allen J. Ellender; (8) Frontiers in World Health (excerpts from address by the Surgeon General; (9) Cooperative Health Programs of the Institute of Inter-American Affairs; (10) list of United States members of the WHO expert committees.

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It contains (1) current information regarding the incidence and geographic distribution of communicable diseases in the United States, insofar as data are obtainable, and of cholera, plague, smallpox, typhus fever, yellow fever, and other important communicable diseases throughout the world; (2) articles relating to the cause, prevention, and control of disease; (3) other pertinent information regarding sanitation and the conservation of the public health.

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Librarians and others should preserve their copies for binding, as the Public Health Service is unable to supply the general demand for bound copies. Indexes will be supplied upon request.

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